Figure 1. Persistence of TCZ Therapy Among All TCZ Initiators, TCZ Initiators Excluding Those With No Reported Reason for Discontinuation and TCZ-IV Initiators

Number of Patients at Risk

1789	1245	861	636	483	378	298
1303	947	663	516	399	318	257
1284	921	644	482	376	307	244

IV, intravenous; TCZ, tocilizumab.

Figure 2. Estimated Effects of Covariates on Duration of TCZ Persistence Among (A) All TCZ Initiators, (B) TCZ Initiators Excluding Those With No Reported Reason for Discontinuation and (C) TCZ-IV Initiators

CDAS, Clinical Disease Activity Score; csDMARD, conventional synthetic disease-modifying antirheumatic drug; IV, intravenous; mDAS, modified Disease Activity Score; RA, rheumatoid arthritis; TCZ, tocilizumab; TNFi, tumor necrosis factor inhibitor. * $P < 0.05$

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FRI0105

EVALUATION OF CXCL13 AND ICAM1 SERUM LEVELS AS PREDICTORS OF CLINICAL RESPONSE TO ABATACEPT IN RHEUMATOID ARTHRITIS.

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Background: Soluble intercellular adhesion molecule 1 (ICAM1) and C-X-C motif chemokine 13 (CXCL13) were described as differentially associated with two major subtypes of synovitis in rheumatoid arthritis (RA). Raised serum levels of ICAM1 (which is upregulated in synovial fibroblasts in response to TNF α), and of CXCL13 (which is expressed by synovial follicular dendritic cells and activated mature antigen-experienced T-helper cells), are associated with a myeloid or lymphoid synovial phenotype, respectively (1). It has been suggested that a preferential clinical response to anti-TNF α , as compared to anti-IL-6R monotherapy, can be predicted by measuring these two biomarkers (2). No information is available on the possible utility of these biomarkers in RA patients treated with abatacept (ABA), a T-cell co-stimulation blocker.

Objectives: To analyze the effect of ABA on ICAM1 and CXCL13 serum levels in RA and to verify whether they predict the response to the drug.

Methods: 63 RA patients [F/M=51/12; median (10th-90th percentile) age=60 (41-72) years; CRP-DAS28=4.6 (3.3-5.8); ACPA positive: 86%], before and after 6 months of treatment with ABA + methotrexate and 22 sex and age-matched healthy controls (HC) were evaluated. Serum ICAM1 and CXCL13 levels were dosed by commercial ELISA (Life Technologies and R&D). Response to treatment was defined with the EULAR criteria.

Results: CXCL13 serum levels were higher in RA at baseline than in HC [136 (42-325) vs 32 (19-57) pg/ml, $p < 0.01$], while no difference was observed in ICAM1 [186 (125-276) vs 184 (153-246) ng/ml, $p = 0.9$]; positive correlations between ICAM1 and CRP ($r: 0.28$; $p = 0.03$) and CXCL13 levels and CRP ($r: 0.40$; $p < 0.01$) and CRP-DAS28 values ($r: 0.27$, $p = 0.05$) were found. After therapy with ABA, a reduction of CXCL13 was observed [136 (42-325) vs 94 (29-319) pg/ml, $p < 0.01$], both in responders [$n: 37$: 151 (57-462) vs 97 (26-329) pg/ml; $p < 0.01$] and non-responders ($n: 14$: 142 (68-293) vs 89 (42-198) pg/ml; $p = 0.01$). Not significant variation of ICAM1 serum levels was found in the entire cohort [186 (125-276) vs 190 (113-252) ng/ml, $p = 0.06$]. However, a significant decrease was observed in non-responders [222 (169-302) vs 186 (110-233) ng/ml, $p = 0.02$]. At baseline, no significant difference was found among patients seropositive for ACPA if compared with the negative ones [ACPA+ vs ACPA- for ICAM1 [187 (123-280) vs 177 (134-258) ng/ml; $p = 0.7$] and for CXCL13 [143 (42-368) vs 113 (56-270) pg/ml; $p = 0.4$].

Conclusion: Our results confirmed that CXCL13 serum levels are directly correlated with disease activity and demonstrated that ABA therapy induces their reduction. These findings suggest that the co-stimulation blockade at central level and/or in the synovium lead to a reduced production of CXCL13. We could not demonstrate that CXCL13 levels predict the clinical response to ABA in this cohort of patients.

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FRI0106

RISK FACTORS FOR SERIOUS INFECTIONS IN PATIENTS WITH RA INITIATING TREATMENT WITH BIOLOGIC DMARDS: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY

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Background: Patients with RA are at increased risk of infection compared with the general population, but it is unclear whether this is due to the underlying disease or to immunosuppressive medications used to manage the disease.¹ Some biologic DMARDs (bDMARDs) have been associated with an increased risk of serious infection.² A large cohort study found no increased risk of serious infection in patients initiating abatacept compared with patients initiating other bDMARDs.³ It is clinically important to identify which patients are at a higher risk of infections at the time of initiating treatment with a bDMARD. However, studies that assess risk factors for infection and derive corresponding risk scores of infection, especially at the time of bDMARD treatment initiation, are lacking or based on too few patients.⁴

Objectives: To identify the risk factors for serious infections among patients with RA initiating treatment with a bDMARD in a real-world observational setting.

Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify patients diagnosed with RA who initiated treatment with a bDMARD between January 2007 and December 2015. Patients were followed from treatment initiation until the occurrence of a serious infection requiring hospitalisation, the end of enrolment or 31 December 2015, whichever came first. The Cox proportional hazards model was used to estimate the hazard ratios (HRs) of serious infection associated with baseline risk factors including demographics, the presence of co-morbidities, prior hospitalised infections and medications. An infection risk score was developed using the independent risk factors found to be significant in the model.

Results: The study cohort included 84,308 patients initiating treatment with a bDMARD, mainly etanercept (36.7%), adalimumab (29.3%), infliximab (12.4%), rituximab (7.3%) and abatacept (6.8%). During a mean follow-up of 6.6 months, 1724 patients were hospitalised for a serious infection (incidence rate 3.7/100 persons per year). The baseline risk factors significantly and independently associated with serious infections were age, prior hospitalisation for infection, hypertension, diabetes, lymphoma, asthma, chronic obstructive pulmonary disease, cardiovascular disease, other autoimmune disease, corticosteroid use and antibiotic use. The infection risk score, with a possible range of 0 to 15, had a mean (SD) value of 2.6 (1.9) with range 0–12.5. The HR (95% CI) of serious infection was 1.43 (1.40–1.45) for every unit increase in the risk score. Relative to patients with a score of 0, the HR (95% CI) of serious infection for a risk score of 5 was 5.9 (5.3–6.5), and for a risk score of 10 was 34.5 (28.5–41.6).

Conclusion: In this large, real-world cohort of patients with RA who were initiating treatment with a bDMARD, several patient characteristics were found to independently predict the subsequent risk of serious infection. The risk score, based on easily available patient characteristics, can be a simple and useful tool for the clinician to identify patients at higher risk of infection at the time of bDMARD initiation for the treatment of RA.

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FRI0107

EFFECTIVENESS OF ABATACEPT ON CLINICAL DISEASE ACTIVITY AND RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS PATIENTS IN DAILY CLINICAL PRACTICE IN JAPAN: COMPARISONS ACCORDING TO ACPA STATUS

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Background: The clinical effectiveness of abatacept (ABA) in rheumatoid arthritis (RA) patients has been reported to be higher when the patients' anti-cyclic citrullinated peptide antibody (ACPA) status is positive. The report from the ORA registry demonstrated that the ACPA positivity was associated with a better response to ABA [1]. In a sub-analysis of the AMPLE trial, patients with very high ACPA titers who were treated with ABA had a statistically significant response compared to patients with lower titers [2]. However, these studies did not demonstrate the data regarding the structural progression.

Objectives: This study aimed to evaluate the effectiveness of ABA on the clinical disease activity as well as the radiographic progression in patients with RA in the clinical settings.

Methods: All eligible patients were registered in the TBCR, a Japanese multicenter registry system for RA patients treated with biologics [3]. The present study included 553 consecutive patients whose ACPA data were obtained, treated with ABA and observed for longer than 52 weeks. We primarily compared the status of disease activity (SDAI) and radiographic progression (van der Heijde modified total Sharp score: mTSS) between ACPA-positive [ACPA (+)] and ACPA-negative [ACPA (-)] RA patients. The ACPA positive was defined as ≥ 13.5 U/ml of anti-CCP antibody.

Results: Number of cases was 446/ 107 [ACPA (+)/ ACPA (-)], respectively. Baseline characteristics between groups were quite similar; mean age was 68.0/ 67.3 years, rate of methotrexate (MTX) use rate was 41.2/ 50.0%, rate of bio-naïve was 28.0/ 31.8%, and mean SDAI score was 22.2/ 20.8. Significant difference was observed in mean change in SDAI score from baseline to 52 weeks between the ACPA (+) and ACPA (-) group (-13.4 vs -9.9, $p = 0.027$) (Figure 1A). Proportion of patients that achieved low disease activity (LDA; SDAI ≤ 11) at 52 weeks was significantly higher in the ACPA (+) group compared to the ACPA (-) group (72.1 vs 56.0%, $p < 0.01$) (Figure 1B). In univariate and multivariate logistic regression analysis, ACPA positivity was an independent predictor for achievement of LDA at 52 weeks (Table). There observed no significant difference between ACPA (+) and ACPA (-) group in the proportion of patients that achieved structural remission (Δ mTSS ≤ 0.5) at 52 weeks (66.2 vs 62.1%) (Figure 2A) as well as mean change in mTSS (1.66 vs 1.17), erosion score (0.60 vs 0.53), and joint narrowing (JSN) score (1.06 vs 0.64) (Figure 2B).

Figure 1

Table.

Variables	Univariate		Multivariate	
	OR (95%CI)	p-value	adjusted OR (95%CI)	p-value
Age	0.99 (0.98-1.01)	0.439	1.00 (0.97-1.02)	0.749
male (vs female)	1.12 (0.70-1.80)	0.634	0.79 (0.40-1.58)	0.511
disease duration	0.99 (0.97-1.00)	0.053	0.99 (0.97-1.01)	0.468
Biologics-naïve	1.23 (0.81-1.85)	0.335	1.18 (0.67-2.08)	0.575
Concomitant MTX use	1.12 (0.75-1.69)	0.585	1.14 (0.66-1.95)	0.649
Concomitant PSL use	0.82 (0.55-1.23)	0.329	0.97 (0.58-1.64)	0.923
SDAI @baseline	0.96 (0.94-0.97)	<0.001	0.96 (0.94-0.98)	<0.001
mHAQ @baseline	0.50 (0.36-0.69)	<0.001	0.57 (0.38-0.86)	<0.001
ACPA positive	2.03 (1.29-3.17)	0.002	2.61 (1.36-5.00)	0.004
			Bold italic, p<0.05	

Figure 2

Conclusion: Consistent with previous reports, the ACPA-positive group demonstrated significantly higher LDA achievement rate at 52 weeks and indeed the ACPA positivity was significantly associated with LDA achievement in multivariate analysis. However, the ACPA-negative group demonstrated quite similar transition of SDAI score and LDA achievement rate except at 52 weeks compared with the ACPA-positive group. Additionally, there was no significant difference in the structural progression at 52 weeks between the groups. ABA treatment